Recent Advances in the Deoxydehydration of Vicinal Diols and Polyols

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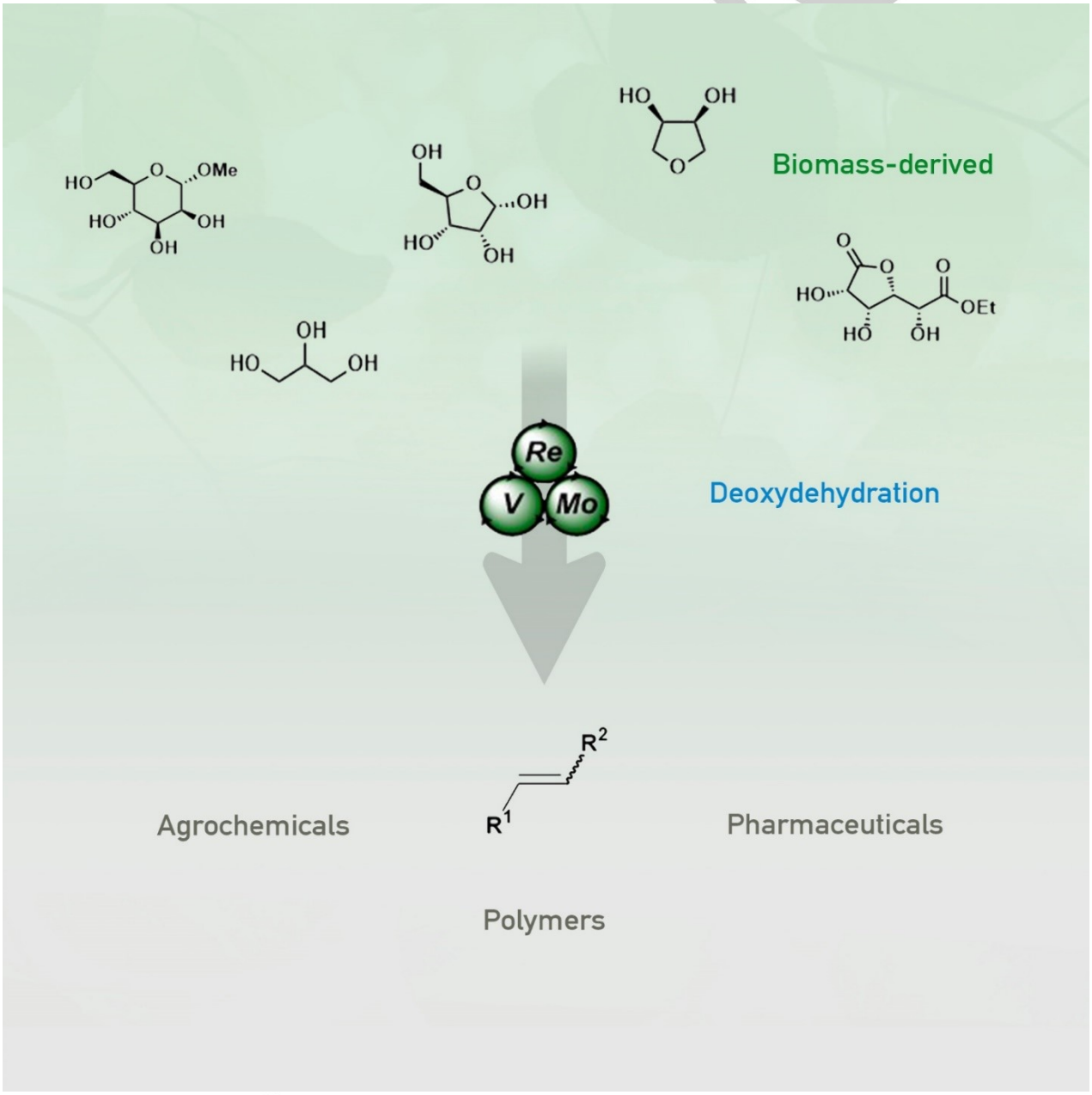
Liam J. Donnelly,[a] Stephen P. Thomas,*[a] and Jason B. Love*[a]



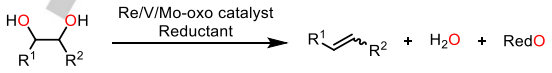
Abstract: Deoxydehydration (DODH) is one of the most promising tools to reduce the oxygen content of biomass (sugars and polyols) and provide analogues of platform chemicals that are derived from fossil resources. This reaction converts a vicinal diol into an alkene and is typically catalyzed by high-oxidation-state metal-oxo compounds in the presence of a stoichiometric reductant, with examples of both homogeneous and heterogeneous systems. This mini-review will highlight the developments in this field over the past 5 years and focus on efforts to solve the problems that currently prevent DODH being performed on a commercial scale, including the nature of the reductant, substrate scope and selectivity, and catalyst recovery and expense.

Introduction

The ever-increasing energy demands of the growing world population along with a current reliance on fossil resources to supply its energy needs means that fossil resources are anticipated to be depleted and are increasingly expensive. The largest projected source of demand for oil over the next two decades is as a feedstock for petrochemicals, primarily driven by the increasing production of plastics.[1] As a carbon-neutral alternative to petrochemical feedstocks, the conversion of biomass into valuable chemicals is may help shape the sustainability of the chemical industry.[2]

There are several challenges that still limit the use of chemicals produced from biomass. Unlike petroleum refineries, biorefineries are not integrated and key primary chemicals and secondary intermediates have not yet been identified. Current biorefineries aim to produce biofuels such as biodiesel and bioethanol which are considered high-volume, low-value products. Biomass-derived feedstocks such as sugars and polyols are carbon-rich, have a high degree of chemical complexity and can potentially be used as precursors to high-value chemicals. However, they are also highly oxygenated which limits their synthetic utility. The conversion of biomass to useful chemicals is therefore reliant on methods that selectively deoxygenate these precursors to access high-value products of industrial relevance. To this end, several methods for reducing the oxygen content in these compounds have been explored, such as, dehydration and hydrodeoxygenation.[3]

In this review we will focus on deoxydehydration (DODH), which can be described as a single-step deoxygenation and dehydration reaction; formally, this involves the loss of one oxygen atom and a molecule of H_2O from a diol to form an alkene. This transformation typically uses an oxo-metal catalyst and an external stoichiometric reductant (Scheme 1). The first example of catalytic DODH was described by Cook and Andrews in 1996 using the oxo-rhenium catalyst, Cp^*ReO_3, and PPh_3 as the stoichiometric reductant to produce the corresponding phosphine oxide as a by-product.[4] The field has experienced renewed interest in the last 10 years as its application in biomass valorization was realized. Rhenium-catalyzed DODH has been extensively studied by several research groups and multiple catalyst/reductant systems have been developed.[5] The choice of reductant is a key part of the DODH reaction and can have profound effects on reaction efficiency and mechanism. Despite the success of rhenium catalysts, it is important to consider cheaper alternatives derived from earth-abundant metals such as V, Mo, and W.[6] Furthermore, DODH reactions are usually conducted at high temperatures (100 – 250 °C) requiring considerations of catalyst stability under these forcing conditions. The ability to separate the catalyst from the product is also an important feature of any DODH system. This mini-review highlights the key recent developments of DODH reactions with a focus on those that address the challenges surrounding the choice of reductant, substrate scope and product selectivity, and the nature of the catalyst with regards to potential application on an industrial scale.



Scheme 1. General reaction conditions for the DODH reaction of a diol to an alkene.

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Liam Donnelly graduated with an MChem. from Nottingham University in 2016, spending a year on placement at Merck, Sharp and Dohme in Hoddesdon working in Process Research. He completed his final year project under the supervision of Hon Wai Lam working on developing a key step in the synthesis of lead-like compounds with known biological activity against tropical diseases such as malaria, in collaboration with GSK research groups at Tres Cantos Open Lab Foundation. Liam then moved to Edinburgh University to begin his PhD studying the chemistry of metal-oxo complexes in reduction catalysis as part of the EPSRC Centre for Doctoral Training in Critical resource Catalysis (CRITICAT).

Stephen Thomas studied chemistry at Cardiff University and completed his PhD with Stuart Warren at the University of Cambridge. After postdoctoral research with Andreas Pfaltz at the University of Basel, Stephen was appointed to a fixed-term lectureship at the University of Bristol associated with Varinder Aggarwal. In 2012 Stephen moved to the University of Edinburgh to a Chancellor's Fellowship and in 2014 was awarded a Royal Society

University Research Fellowship. Stephen was awarded the 2016 RSC Hickinbottom Award, a 2017 Thieme Chemistry Journals Award and a 2018 Pfizer Green Chemistry Research Award.

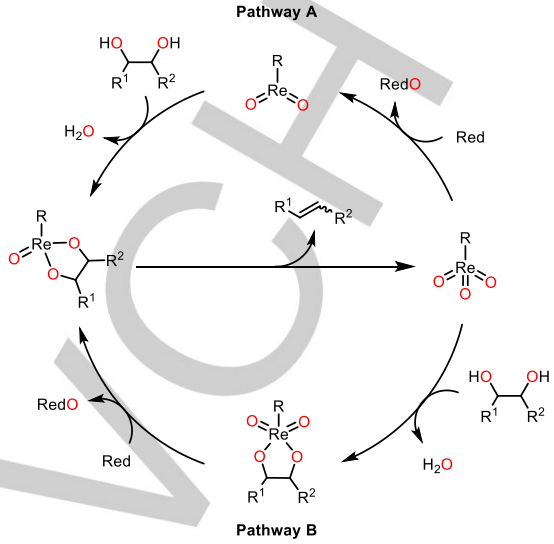
Jason Love was awarded a BSc (Hons) in Applied Chemistry by Salford University in followed by a PhD in rhenium polyhydride chemistry with John Spencer. After postdoctoral positions with Geoff Cloke (Sussex), Michael Fryzuk (Vancouver), and Martin Schröder (Nottingham) he was awarded a lectureship and Royal Society URF at Sussex in 1999. He moved to Nottingham University and then to Edinburgh University where he is currently Professor of Molecular Inorganic Chemistry. He studies the chemistry of small molecule redox catalysis in relation to chemical sustainability, f-element chemistry, supramolecular catalysis, and metal recycling.

Rhenium Catalysts

Following the renewed interest in DODH, oxorhenium complexes have been the most widely investigated and efficient catalysts reported. The mechanism of the Re-catalyzed reaction has been studied extensively in both experimental and computational investigations. These investigations have led to the general conclusion that the reaction proceeds by condensation of the diol to the rhenium center, oxidative extrusion of the alkene and two-electron reduction of rhenium. The discussion surrounding the mechanism has focused upon whether the reduction step proceeds before the condensation step (Scheme 2, pathway A) or after the condensation step (Scheme 2, pathway B). The order of events appears to be heavily influenced by the choice of catalyst and reductant. The efforts to understand this key step have been highlighted in previous reviews and will therefore not be discussed in detail in this work.[5]

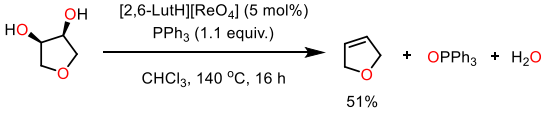
CATALYSTS – LIGANDS

Early DODH procedures employed methyltrioxorhenium (MTO) as the catalyst, but in recent years MTO has fallen out of favor due to its relatively high cost and poor thermal stability. Klein Gebbink and co-workers have reported the synthesis of a range of cyclopentadienyl trioxorhenium complexes and examined their competency as catalysts in DODH reactions.[7] Bulky electron-rich Cp' ligands were designed to suppress over-reduction of rhenium and the formation of catalytically inactive dimeric species.[8] An initial screen of these complexes showed that $Cp^{tt}ReO_3$ (Cp^{tt} = 1,3-di-*tert*-butylcyclopentadienyl) exhibited the highest catalytic activity and a relatively short induction period. Under optimized conditions using 2,4-dimethyl-3-pentanol (DMP) as both solvent and reductant, glycerol was converted to allyl alcohol in 90% yield with exceptionally low catalyst loadings (0.1 mol%, TON 900).[9] *In situ* NMR spectroscopy revealed that the Cp' ligands readily dissociate under reactions conditions and the rate of dissociation is linked to the catalyst induction period, where fast dissociation leads to a shortened induction period.



Scheme 2. Proposed mechanisms for Re-oxo catalysed DODH.

Love and co-workers have shown that simple pyridinium perrhenate salts can catalyze the DODH of a variety of diols to alkenes using PPh_3 as a stoichiometric reductant.[10] A range of pyridinium catalysts were synthesized in one step from perrhenic acid and screened in the DODH of styrene glycol using 5 mol% of catalyst in $CHCl_3$ at 90 °C (Scheme 4). Lutidinium perrhenate was used as the catalyst to expand the substrate scope to other polyols due to having high activity and good solubility in organic solvents. The biomass-derived diol 1,4-anydroerythritol was converted to 2,5-dihydrofuran in 51% yield at 140 °C. The pyridinium cation acts as a Brønsted acid in a proton-shuttling mechanism, enabling the reaction to be conducted at significantly lower temperatures (90 °C) than previously reported systems (130 – 250 °C). Pyridines are known to coordinate to Re(V) oxo species in DODH catalysis, leading to catalyst inhibition.[11] This effect was evaluated by DFT calculations and shows that as the steric bulk of the coordinating amine/pyridine increases, the stability of the Re(OH)(O)(diol)(L) (L = amine or pyridine) that is formed off-cycle, decreases.

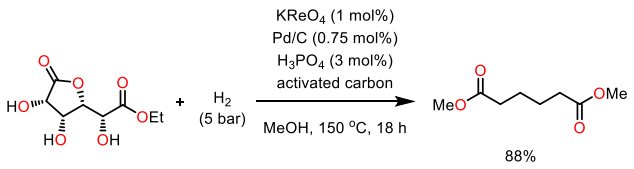


Scheme 3. Lutidinium perrhenate catalysed conversion of 1,4-anhydroerythritol to 2,5-dihydrofuran.

GLYCEROL, ADIPATES and 5-(HYDROXYMETHYL)FURFURAL

The DODH of biomass-derived sugar acids into industrially relevant saturated carboxylic acids is an attractive prospect and has been the focus of a number of research groups. The

development of a scalable system for the production of adipic acid, which is used on a megatonne scale for the production of nylon-6,6, from sustainable sources is of particular interest as the current industrial process relies on petroleum-derived starting materials.[12] The groups of Su and Zhang have shown that a one-pot MTO-catalyzed DODH of mucic acid and subsequent Pt/C-catalyzed transfer hydrogenation gave a mixture of adipic acid esters in near quantitative yield, which can then be hydrolyzed to the free acid.[13] The DODH reaction was conducted at 120 °C with 5 mol% MTO, 5 mol% of TsOH co-catalyst, and 3-pentanol as the reductant for both the DODH and hydrogenation steps. The reaction can either be conducted as a one-pot, one-step or one-pot, two-step procedure; however, the former reaction leads to a significantly reduced yield of 75% compared to 99% for the two-step procedure. DFT calculations of this reaction proposed that MTO is reduced to $MeRe(OH)_2O$ prior to condensation with the diol. The second DODH reaction was proposed to proceed at a faster rate than the first DODH reaction.



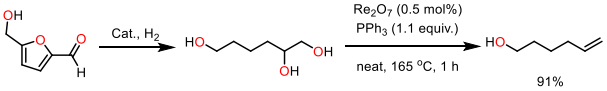
Scheme 4. Tandem DODH/hydrogenation of glucarates to adipates.

Toste and co-workers have developed a related procedure for the one-pot, one-step DODH and hydrogenation of glucarates to adipic acid.[14] A bimetallic catalyst system of $KReO_4$ (1 mol%) and Pd/C (0.75 mol%) using H_2 as the stoichiometric reductant and MeOH as solvent produced the methyl adipate ester in 61% yield. This yield was improved to 88% by addition of H_3PO_4 (3 mol%) to facilitate ring-opening of the lactone intermediates, and activated carbon (27 wt%) which could act as a support for reduced Re species (Scheme 4). The substrate scope was expanded to other biomass-derived lactones and sugar acids/esters. Under these conditions high selectivity from vicinal diols that are *adjacent to the carbonyl functionalities* in the presence of 'unactivated' diols was observed. This is thought to occur due to the electron-withdrawing nature of the carboxylate groups which lowers the energy of the transition state for C-O bond cleavage and alkene extrusion.

Glycerol is a by-product in the production of soaps and biodiesel through the transesterification of triglycerides. Glycerol supply has increased well beyond the point of demand in recent years, to the point where most of it is disposed of by burning. This presents glycerol as an ideal candidate for deoxygenation to more valuable commodity chemicals.[15] d'Alessandro and co-workers developed a process for the disproportionation of neat glycerol to allyl alcohol and dihydroxyacetone using either ReO_3 or MTO (2 mol%) as catalyst.[16] When H_2 was bubbled through the reaction mixture at 140 °C, an allyl alcohol yield of 34% was achieved in 16 hours, with no observed formation of acrolein, diallyl ether or allyl formate. The volatile products were collected in an aqueous ice-cooled trap. The reaction could also be conducted in alcoholic solvent with H_2 bubbling leading to the formation of allyl alcohol in 91% yield with trace amounts of acrolein produced. NMR reactions with MTO as catalyst revealed complete demethylation of MTO in <1 hour under the reaction conditions, which coincided with an induction period for allyl alcohol formation. This result suggests that MTO acts a pre-catalyst for the formation of ReO_3 or related ReO_x polymers.

This process was studied further by d'Alessandro and Marrone to elucidate the identity of the active catalyst by screening a range of rhenium complexes (oxo, halo, phosphino) in catalysis.[17] In either neat conditions or with DMP as solvent the formation of a Re-alkoxide precipitate was observed in all cases, concomitant with an induction period in the kinetic profile of the DODH reaction. The isolated precipitate was a competent catalyst for the DODH of glycerol with no observed induction period.

Wozniak and coworkers have examined the DODH of triols that are derived from chemical 5-(hydroxymethyl)furfural (HMF), which is a prominent chemical derived from carbohydrates.[18] HMF can undergo hydrogenation to provide either 1,2,5-hexanetriol (1,2,5-HT) or 1,2,6-hexanetriol (1,2,6-HT) which were tested under DODH conditions. 1,2,6-HT can be converted to 5-hexen-1-ol in 91% isolated yield using Re_2O_7 (0.5 mol%) as the catalyst and PPh_3 as the reductant at 165 °C for 1 hour under neat conditions (Scheme 5). Unfortunately, reductants other than PPh_3 proved ineffective and over-reduction of Re_2O_7 was observed by formation of a black, insoluble precipitate during catalysis. It was possible to recycle the catalyst by carefully tuning the stoichiometry of PPh_3 in the reaction. When the reaction was conducted under an Ar atmosphere instead of air the yield was reduced to 65%, which suggests that oxygen plays a role in catalysis. 1,2,5-HT showed poor selectivity for 5-hexen-2-ol under similar conditions and instead undergoes dehydrative cyclisation to 5-methyltetrahydrofurfuryl alcohol (5-MTHFA) in the absence of PPh_3. A one-pot DODH hydrogenation reaction was also developed for 1,2,6-HT giving a 51% yield of 1-hexanol with Re_2O_7 (5 mol%) and Ru/C (10 mol%) under a H_2 atmosphere (30 bar) at 165 °C in THF.



Scheme 5. DODH of the 5-HMF derived 1,2,5-HT to 5-hexen-1-ol.

REDUCTANT

The choice of reductant is key to the efficiency of any DODH system and can have a significant effect on the reaction mechanism. The use of elemental reductants (Zn, Fe, Mn, C) was studied by Nicholas and co-workers in the DODH of model biomass polyols using NH_4ReO_4 (10 mol%) at 150 °C in benzene with two equivalents of reductant.[19] These conditions enabled the conversion of 1,2-decanediol to 1-decene in 34 - 69% yield in 24 hours. The advantage of using elemental reductants such as Zn is that the oxidized products do not dissolve in the reaction solvent and can be easily separated from the alkene product. It is necessary to use two equivalents of reductant to account for competing oxidation by oxygen, as exhibited by a yield of 56% with 1.1 equivalents of Zn and 68% with 2 equivalents. Other non-

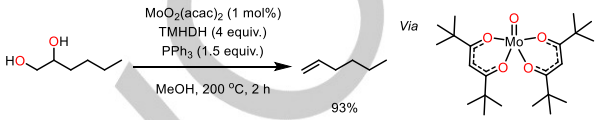
aliphatic diols were tested under these reaction conditions. 1-Phenyl-1,2-ethanediol was converted to styrene in 85% yield with 1.1 equivalents of Zn, and diethyl tartrate (DET) was cleanly converted to diethyl fumarate (DEF) in 84% yield with 2 equivalents of Zn.

Nicholas has also shown that fossil-derived dihydroaromatics (DHAs) can be used as H_2 surrogates in DODH reactions.[20] Several DHAs were screened as reductants in the DODH of DET and 1,2-octanediol with NH_4ReO_4 as the catalyst (10 mol%) at 150 °C for 48 hours with either toluene or benzene as solvent. The highest yields of deoxygenated products were achieved when indoline (1.1 equivalents) was used as the reductant, with DEF and 1-octene formed in yields of 99% and 70% respectively. Yields for a variety of diols and polyols ranged from 35% to 99% using either NH_4ReO_4 or MTO as the catalyst. Competition experiments with 2-butanol and 3-pentanol showed that indoline out-competes alcohols as the reductant by quantifying the amount of ketone or indole formed at the end of the reaction. Stoichiometric reactions of indoline with MTO formed the *N*-coordinated MTO/indoline complex, which was characterized by single crystal X-ray crystallography. Upon heating this complex indoline was fully consumed after 4.5 hours with formation of indole.

Molybdenum Catalysts

In addition to Re catalysts, less expensive, more earth-abundant metals have been explored as catalysts for DODH reactions. Fristrup and co-workers reported molybdenum-catalyzed DODH using ^{i}PrOH as both solvent and reductant. The inexpensive and commercially available $(NH_4)_6Mo_7O_{24}.4H_2O$ (AHM) was used as the catalyst (10 mol%) in the DODH of 1,2-decanediol at 240-250 °C in ^{i}PrOH to yield 1-decene as the major product in 49% yield.[21] The addition of Bu_4NOH (15 mol%) as a co-catalyst led to an increase in yield to 55%, presumably through its role in solubilizing the inorganic Mo salts. When glycerol was subjected to these reaction conditions it was converted to propylene in 19% yield, allyl alcohol in 4% yield and trace amounts of 1,5-hexadiene. Allyl alcohol was confirmed to be an intermediate in the formation of propylene from glycerol through sequential DODH and deoxygenation. The DODH of sugar alcohols was also conducted, with erythritol yielding 39% of 2,5-dihydrofuran in the absence of Bu_4NOH and 1,4-anydroerithrytol forming 2,5-dihydrofuran in 75% yield. DFT calculations of the reaction of 1,4-anhydroerythritol with MoO_3 suggested that condensation of the diol occurs before reduction of Mo^{VI} to Mo^{IV} by transfer hydrogenation with ^{i}PrOH. Alkene extrusion occurs by a retro-[3+2]-cycloaddition from the diolate species. These calculations also point to the reduction of Mo to be turnover-limiting in this reaction.

De Vos and co-workers sought to improve the stability of Mo catalysts by synthesizing Mo complexes with bulky β-diketonate ligands to prevent oligomerization of the Mo species present during catalysis, which would otherwise lead to catalyst precipitation.[22] Multiple β-diketonates of varying steric and electronic properties were tested as ligands in the DODH of 1,2-hexanediol using $MoO_2(acac)_2$ as pre-catalyst at 200 °C in mesitylene using PPh_3 as the reductant (Scheme 6). Increasing the steric bulk and electron-donating strength of the β-diketonate ligands had a positive effect on the yield of 1-hexene formed. The highest 1-hexene yield of 36% was achieved using 2,2,6,6-tetramethylheptanedionate (TMHD) as ligand, compared to a yield of 15% without any additional ligand. The formation of $MoO_2(TMHD)_2$ was observed under these reaction conditions as well as dimeric complexes. By increasing the addition of TMHD to 4 equivalents the yield of 1-hexene were increased to 93% in 2 hours.



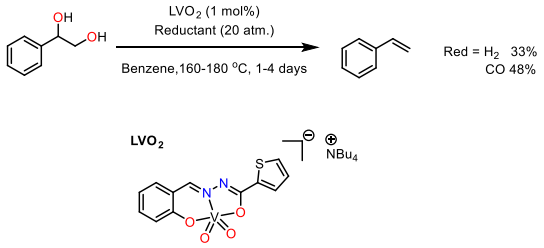
Scheme 6. Mo-catalysed DODH of 1,2-hexanediol to hexene using the bulky TMHDH ligand.

Palkovits and Okuda reported the first example of a heterogeneous DODH catalyst not based on Re.[23] The *in situ* formation of a MoO_x/TiO_2 catalyst from AHM and TiO_2 showed good catalytic activity for the DODH of 1,4-anhydroerythritol using 3-octanol as the reductant at 200 °C, giving 2,5-dihydrofuran in 76% yield. The catalyst was also able to be recycled up to 5 times with no significant loss in activity and leaching of catalytically active species into the reaction medium was not observed under these conditions. However, this system suffers from the formation of side-products under the reaction conditions; ketal formation was observed through the condensation of 1,4-anhydroerythritol with 3-octanone, and octenes were formed through the dehydration of 3-octanol. Contrary to other Mo-catalyzed systems, analysis of different MoO_x/TiO_2 catalysts showed that samples with a high degree of polymerization exhibit higher catalytic activity compared to catalysts with more isolated molybdate species.

Vanadium Catalysts

Nicholas and Gopaladasu synthesized four oxo-vanadium complexes, $[Z][VO_2(L)]$ (Z = cation; L = ligand), and tested their activity in the DODH of a variety of polyols.[24] It was found that $[NBu_4][VO_2(Salhyd)]$ (Scheme 7) was an effective catalyst for the DODH of styrene glycol using inexpensive and readily available H_2 or CO as the reductant. Styrene was formed in 33% and 48% yield with H_2 and CO respectively, at 160 °C in benzene with no observed over-reduction to alkene products observed when H_2 was used. The difference in reactivity of the salhydrazide complex was attributed to its relatively high basicity which makes reduction of V^{V} harder but oxidation of V^{III} species easier. Stoichiometric reactions of $[NBu_4][VO_2(Salhyd)]$ with CO resulted in a color change from yellow to green and the formation of a paramagnetic species, with IR spectroscopy suggesting the presence of a bridging CO ligand. No reaction with CO was observed in the

analogous stoichiometric reactions with the other Z[VO_2(L)] complexes.



Scheme 7. DODH of styrene glycol using [NBu_4][VO_2(Salhyd)] as catalyst.

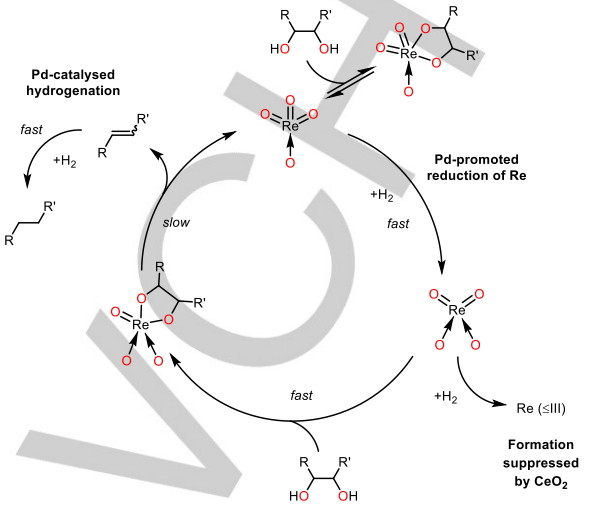
The simple and commercially available ammonium metavanadate (NH_4VO_3) was evaluated as a catalyst for the conversion of glycerol to allyl alcohol by Fristrup and co-workers, giving comparable yields and selectivities to the analogous MTO catalyzed reaction, albeit at significantly higher temperatures; the reaction was conducted under solvent-free conditions at 250 °C in 5 hours with 1 mol% catalyst to give an allyl alcohol yield of 22%. No H/D scrambling was observed when deuterium labelled glycerol was used in the reaction. These mechanistic studies support a DODH pathway to allyl alcohol production and acrolein formation by consecutive dehydration steps.

Heterogeneous Rhenium Catalysts

While the majority of reported systems for DODH catalysis are homogeneous there has been emerging interest in using heterogeneous catalysts, primarily based on rhenium, for this reaction.[26] The advantages of using heterogeneous catalysts includes ease of separation from the reaction mixture and improved catalyst stability at high temperatures. Palkovits and co-workers reported a ReO_x/TiO_2 catalyst, formed from NH_4ReO_4 and TiO_2 at 300 °C under an atmosphere of H_2, for the DODH of a variety of glycols including glycerol;[25] the reaction was conducted at 170 °C for 1 hour using 3-octanol as the reductant and 5 wt% of the supported Re catalyst. The catalyst was recycled up to 6 times without any significant loss in activity in the conversion of 1,2-hexanediol to 1-hexene. XAS analysis of the catalyst material showed a mixture of Re^{VII}, Re^{IV} and Re^0 oxidation states. After catalysis a 10% increase in the amount of Re^{VII} was observed but no further change in catalyst composition was seen after multiple recycling reactions.

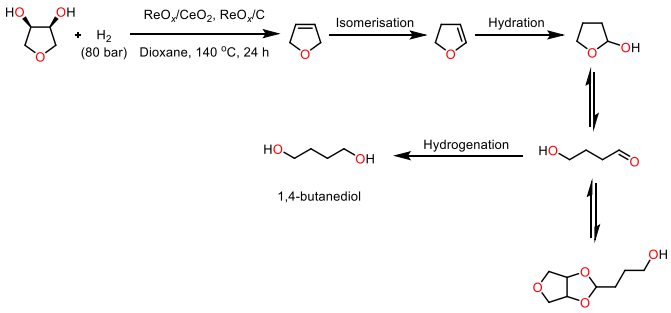
The one-pot deoxydehydration/hydrogenation of glycols to alkanes was reported by Tomishige and co-workers using a ReO_x-Pd/CeO_2 (2 wt% Re, 0.3 wt% Pd) catalyst and H_2 as the reductant for both steps.[26] Using this catalyst, 1,4-anhydroerythritol was converted to THF at 300 °C in dioxane in a yield of <99% after 64 hours; however, similar catalytic reactions with other substrates suffered from poor selectivity. After reduction, the ReO_x-Pd/CeO_2 material mostly comprised Re^{IV} species and after stoichiometric reaction with 1,2-hexanediol a portion of Re^{IV} was converted to Re^{VI} with the amount of Re^{IV} converted corresponding to the amount of 1-hexene produced.

The role of Pd is to promote reduction of Re^{VI} to the active Re^{IV} centers. The CeO_2 support stabilizes the Re^{IV} species and prevents over-reduction by H_2 (Scheme 8).[27]



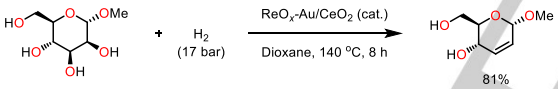
Scheme 8. Proposed reaction mechanism for ReO_x-Pd/CeO_2 catalyzed tandem DODH/hydrogenation of glycols.

In contrast to the above Pd-containing catalyst, Tomishige and Nakagawa have also shown that a ReO_x-Au/CeO_2 catalyst can be used to convert glycerol to allyl alcohol in 91% yield without any significant amount of over-reduction to 1-propanol.[28] The Au promoter activates H_2 to reduce the Re to catalytically active species. Alkene hydrogenation, isomerization and migration reactions are suppressed in the presence of polyol due to competitive binding to the catalyst; however, once the starting material has been consumed these side-reactions become more pronounced. Differences in reactivity were observed for different Au loading methods; impregnation provided larger Au particles (~12 nm) that were less able to activate H_2 activation compared with deposition-precipitation which provided smaller particle sizes (~3 nm).[29] A co-catalytic monometallic system for the conversion of 1-4-anhydroerythritol to 1,4-butanediol was also reported and adopts a DODH / isomerization / hydration / hydrogenation pathway (Scheme 9).[30] ReO_x/CeO_2 in combination with ReO_x/C-BP as catalysts provided 1,4-butanediol in 89% yield under an atmosphere of H_2 at 140 °C in dioxane. This dual Re system eliminates the need for the Au promoter as it is now possible to access high oxidation-state Re to perform the DODH reaction and low oxidation state Re to activate H_2.[33]



Scheme 9. Synthesis of 1,4-butanediol from 1,4-anhydroerythritol through a DODH/isomerisation/hydration/hydrogenation pathway.

DODH reactions are typically limited to the formation of structurally simple products and generally leads to the intrinsic stereochemistry of the starting material being lost in this product. Sugars are one of the most stereocomplex biomass-derived chemicals and have been used as chiral pool starting materials for the synthesis of a number of high-value chemicals.[31] Tomishige and Tamura used a ReO_x-Pd/CeO_2 catalyst to selectively deoxygenate methyl-glycosides through DODH of *syn*-vicinal OH groups and subsequent hydrogenation to give dideoxyglycosides, with retention of the stereocenters from the starting material that are not converted to alkenes (Scheme 10).[35] ReO_x-Au/CeO_2 was used in a similar strategy as previously described to avoid hydrogenation of the DODH products allowing the synthesis of unsaturated products from methyl glycosides in up to 88% yield.



Scheme 10. DODH of methyl *α*-D-mannopyranoside with retention of stereochemistry

Similar to the homogeneous system reported by Toste and co-workers,[14] Deng and Wang have shown that zirconia supported rhenium oxide, ReO_x/ZrO_2, catalyses the DODH of D-glucaric acid to the corresponding alkenyl dibutyl adipate esters using *n*-butanol as reductant to give a combined yield of 93%.[36] It was found that changing the support had a significant effect on the reducibility of the ReO_x species, with ZrO_2 providing favourable weak interactions with ReO_x, allowing the reaction to be conducted under relatively mild conditions (140 °C). When ReO_x-Pd/CeO_2 was combined with Pd/C for subsequent hydrogenation of the alkenyl products to give the corresponding adipic acid ester in 82% yield.

Abu-Omar and Delferro reported the synthesis of unsupported rhenium oxide nanoparticles (ReO_x NPs) from NH_4ReO_4 and 3-octanol under reflux and their application in DODH catalysis.[33] Glycerol was converted to allyl alcohol in 76% yield in 3-octanol at 170 °C after 10 h. A hot flitration test showed that the active catalyst is heterogenous and no significant leaching of the catalyst to 3-octanol was observed, allowing the catalyst to be recycled up to 7 times with no loss in activity. The predominant oxidation-states of Re in the ReO_x NPs before catalysis was Re^{VII} with structures similar to perrhenate, after catalysis partial reduction of Re centres to Re^{V} is observed and a higher ratio of Re^{V} and Re^{VII} to lower oxidation-states corresponds to higher catalytic performance. Deuterium labelling experiments showed a large KIE for 3-*d*-octanol indicating that C-H activation during Re reduction is involved in the rate-limiting step.

Summary and Outlook

The development and understanding of new homogeneous Re catalysts has been the focus of several research groups and new ligand architectures have been designed that improve catalyst stability and efficacy; however, rhenium is an non-sustainable metal, and further work is needed to enhance its recovery and recycling from the reaction mixture. In contrast, heterogeneous catalysts are straightforwardly separated from the reaction medium and a variety of new catalytic systems has been reported for the efficient DODH of glycols, as well as tandem DODH/hydrogenation reactions to give alkane products. Even so, to improve the sustainability of DODH processes it would be advantageous to replace Re catalysts with inexpensive and earth-abundant metals such as V and Mo. There are a number of examples of effective catalysts based on V and Mo, but these systems suffer from forcing reaction conditions, such as very high temperatures, and are not effective for the DODH of more challenging substrates such as biomass-derived sugars.

The DODH of biomass-derived glycols is typically designed to produce commodity chemicals or intermediates. The DODH of glycerol is a prime of example of taking a low-value waste product and converting it to higher-value bulk chemicals such as allyl alcohol or acrolein. Another attractive approach is the conversion of biomass-derived sugars to high-value synthons for applications in the pharmaceutical, agrochemical and fine chemicals industries by retaining their inherent stereochemistry through selective deoxygenation. Such transformations can add considerable value to DODH catalysts and expand the scope of this transformation.

The choice of reductant can have a significant effect on the yield and selectivity of DODH reactions, but the price and environmental impact of the reductant must also be considered to develop sustainable and scalable processes. PPh_3 is a very effective reductant but suffers from being expensive, and unless the phosphine can be easily recycled it is unlikely to be applied on an industrial scale. Cheap and readily available secondary alcohols have also been used as reductants, although the corresponding ketones are reactive and can engage in side reactions, and the alcohols themselves can form esters with carboxylic acids. H_2 is the simplest and most economical reductant for the DODH reaction producing H_2O as the by-product, yet there are few examples of effective DODH catalysts which utilize H_2. The main challenges remaining for reductant choice are in separation of oxidized reductant from the DODH product and limiting over-reduction of the catalyst to inactive metal complexes of lower oxidation states.

Research in the field of DODH has progressed rapidly over the past five years with exciting developments in catalyst design, substrate scope and sustainability. However, significant challenges remain before DODH processes can be considered as industrially viable. The use of Re catalysts must be addressed by catalyst recovery and reuse or by replacing these with catalysts derived from earth-abundant metals. The issues associated with the stoichiometric reductant will need to be mitigated, potentially by using a catalytic reductant that can be regenerated under the reaction conditions. The field of DODH still presents many opportunities for process optimization and, furthermore, the study of the mechanism of this reaction may provide chemical insight for the development of new homo- and heterogeneous catalyst systems.

Acknowledgements

The authors thank the University of Edinburgh and the EPSRC CRITICAT Centre for Doctoral Training (Ph.D. studentship to L.J.D; Grant EP/L016419/1) for financial support. SPT thanks The Royal Society for a University Research Fellowship.

Keywords: biomass • DODH • sustainable chemistry • catalysis • metal-oxo

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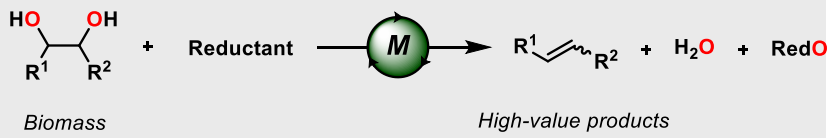
Layout 2:

MINIREVIEW



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A mini-review on the current state of the art in metal-catalysed deoxydehydration of diols is presented with an analysis of current and future challenges in this area.

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Recent Advances in the Deoxydehydration of Vicinal Diols and Polyols